MeritCare Health System

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Aunt Cathy's Guide To:
All Those Lipids

Recommendations for Using Different Types of Vegetable Oils (Omega-3, Omega-6 and Monounsaturated Oils)

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Practical Applications: The Bottom Line
(Subject to change at any moment! ☺):

1. **When buying margarine and shortening, look for some brands that are now available labeled "free of trans fatty acids."** Trans fatty acids are formed as a by-product of the process that produces "partially hydrogenated" vegetable oils – which converts the liquid oils to a more solid, spreadable texture. The trans fats seem to be as bad (or worse) for the heart as "saturated" fats like lard and coconut oil in terms of causing a person's body to produce more cholesterol. It also is a factor in whether or not the cholesterol in the blood "sticks" to the inside of arteries and clogs things up. Other health problems are being identified as well. High consumption of trans fat is associated with increased inflammation and high "oxidative stress" in humans. This could increase the risk of the development or acceleration of several diseases, such as cancer, atherosclerosis, and type 2 diabetes, and a possible increased risk of infertility. (Am J Clin Nutr. 2007 Jan;85(1):231-7. Am J Clin Nutr. 2006 Nov;84(5):981-8. J Nutr. 2005 Mar;135(3):562-6.)

   Some new techniques for making margarine and shortening from vegetable oils do not cause trans fatty acids to be formed at all, so look for the phrase "no trans fat" on the label. Starting January 2006, a law went into effect requiring the trans fat content to appear on the label. This requirement is stimulating research by food producers to explore more ways to prepare foods without trans fat. Foods produced prior to this date will still be able to have undisclosed trans fat.

   Foods may be labeled "No Trans Fat" if they contain less than a gram per serving, so the better way to be sure to minimize intake of trans fat is to also **look on the ingredient list for the words "partially hydrogenated."** In addition to trans fats that we might add to our foods, the ingredient list of many commercially made baked goods and other commercial foods also need to be looked at. Removing trans fat from our food supply is the goal and it is a work in progress. Until it is gone we should read ingredient lists carefully.

2. **Nuts and peanuts are generally friendly in terms of the type of fat they contain, and they also are great sources of important minerals like magnesium and other goodies.** Like other foods that contain a generous amount of fat, nuts and peanuts are high calorie foods, but the forms of fat they contain appears to be **primarily dangerous to your width and not to your heart!** In other words, the calories they contribute may be a problem for people who are aiming to take in fewer calories, but the form of fat is not as contributory to health problems as certain other forms of fat are. It now appears that besides not contributing to the risk of heart disease and cancer, **adding nuts and legumes to the diet can actually be a tool to decrease the risk.**

   Nuts and legumes tend to have good proportion of the fat as **monounsaturated fat**, and of the polyunsaturated fats a reasonable ratio of omega-6 to omega-3 fat. (More on that topic will follow.) A large Harvard study of women followed for 16 years, **eating nuts or peanuts four or more times a week was associated with a 25% decreased risk of developing diabetes** compared with women who rarely ate them. A recent review of research studies found that nut consumption can actuallylower bad cholesterol (LDL) more than following a diets that are "low fat" and nuts can be an excellent food in the fight against what is called "metabolic syndrome."

   [Edible nuts and metabolic health. Curr Opin Lipidol. 2007 Feb;18(1):25-30. Tree nuts and the lipid profile: a review of clinical studies. Br J Nutr. 2006 Nov;96 Suppl 2:S68-78. Nut and peanut butter consumption and risk of type 2 diabetes in women. JAMA. 2002;288(20):2554-60. Effect of diets enriched in almonds on insulin action and serum lipids in adults with normal glucose tolerance or type 2 diabetes. Am J Clin Nutr. 2002;76(5):1000-6. Evidence-based dietary recommendations for patients with type 2 diabetes mellitus. Nutr Clin Care. 2003;6(2):51-61.]

   Peanuts were counted separately in the study of likelihood of developing diabetes because they are really not a nut but a member of the bean (legume) family. However, both had the same apparent beneficial effect. Note that both nuts and legumes are excellent sources of fiber and important nutrients like magnesium and chromium, which also are especially important in diabetes. The fat, protein, fiber, and vitamin/mineral content are all part of that complex puzzle, but the bottom line is that it is good to include nuts and legumes in one's diet.

   [Role of cellular magnesium in health and human disease. Front Biosci. 2004 Jan 1;9:262-76. Magnesium intake and risk of type 2 diabetes in men and women.Diabetes Care. 2004 Jan;27(1):134-40. Dietary magnesium intake in relation to plasma insulin levels and risk of type 2 diabetes in women. Diabetes Care. 2004 Jan;27(1):59-65. The association between magnesium intake and fasting insulin concentration in healthy middle-aged women. J Am Coll Nutr. 2003 Dec;22(6):533-8.Low plasma magnesium in type 2 diabetes. Swiss Med Wkly. 2003 May 17;133(19-20):289-92. Magnesium deficiency in African-Americans: does it contribute to increased cardiovascular risk factors? J Natl Med Assoc. 2003 Apr;95(4):257-62. Oral magnesium supplementation improves insulin sensitivity and metabolic control in type 2 diabetic subjects: a randomized double-blind controlled trial. Diabetes Care. 2003 Apr;26(4):1147-52. Role of magnesium in insulin action, diabetes and cardio-metabolic syndrome X.Mol Aspects Med. 2003 Feb-Jun;24(1-3):39-52.]

   (Please see "Aunt Cathy's Guide to Nutrition: Magnesium and Chromium" and "Aunt Cathy's Guide to OTHER Nutrition Issues in Diabetes" if you want details about their role in diabetes.)

3. **For cooking and baking, canola oil, olive oil, non-hydrogenated soy oil and walnut oil are best and they appear to be better for you than corn oil.** They all contain the same amount of calories – about 9 calories per gram, or about 100 per tablespoon. But both have better proportions of the "friendlier" oils (monounsaturated and omega-3 polyunsaturated fats); corn oil is almost all the "omega-6" kind of fat. The reason for this is explained more fully below.

4. **Adding ground flax to foods is also good for you**. It needs to be ground up, though (or purchased that way -- you can get it at most grocery stores now) because otherwise the intact flax seeds just pass right on through like a high fiber supplement, and the good stuff inside is not absorbed into the body. Use a coffee grinder if you want to grind whole flaxseeds at home – the tiny seeds just jump over the blades in a regular food processor. The generous amount of

"friendly" fat in flax is an omega-3 fat called "alpha-linolenic acid." Ground flaxseeds can be added to hot or cold cereal or granola, or used in muffins, pancakes, meatloaf, etc. Some ready-to-eat cereals are now available that have ground flaxseed in them; some have the whole intact seeds in them so they may be less helpful. Most ground flax products are best stored in the refrigerator or they can turn rancid**.**

It appears that the ground flaxseed is more beneficial than taking the flax oil in capsules, probably because of the micronutrients and the fiber. A fiber-like material in the seeds called "lignins" appears to have health benefits as well. Soybeans and walnuts will also provide many additional nutrients besides "friendly" fat.

[Supplementation with flaxseed alters estrogen metabolism in postmenopausal women to a greater extent than does supplementation with an equal amount of soy. Am J Clin Nutr. 2004; 79(2):318-25. Flaxseed and cardiovascular risk. Nutr Rev. 2004;62(1):18-27. Flax facts. A grain for good health. Diabetes Self Manag. 2003;20(6):18, 20-2. The effect of flax seed cultivars with differing content of alpha-linolenic acid and lignans on responses to mental stress. J Am Coll Nutr. 2003;22(2):157-64. Dietary flaxseed meal is more protective than soy protein concentrate against hypertriglyceridemia and steatosis of the liver in an animal model of obesity. J Am Coll Nutr. 2003 ;22(6):494-501.]

5. **Eat fish when able (avoiding the swordfish and other big fish known to contain high levels of mercury), and consider taking a couple of fish oil capsules daily, especially if you do not eat fish.** This has to do with trying to eat more oils from the "omega-3" family and less from the "omega-6" family. **Taking in the <u>forms</u> of omega-3 oils in fish (EPA and DHA) has certain advantages over only eating the plant/vegetable form (linolenic acid.)** There is more on this topic later. The fish oil supplements are less likely to contribute mercury in part because the mercury tends to be distributed mostly in the flesh of the fish and not as much in the fat. Also, various treatments are used to make the capsules safer. There is a table on Page 8 that shows the amount of omega-3 fat in oils, flax and fish.

[Measurement of organochlorines in commercial over-the-counter fish oil preparations: implications for dietary and therapeutic recommendations for omega-3 fatty acids and a review of the literature. Arch Pathol Lab Med. 2005 Jan;129(1):74-7. Measurement of mercury levels in concentrated over-the-counter fish oil preparations: is fish oil healthier than fish? Arch Pathol Lab Med. 2003 Dec;127(12):1603-5. Mercury, fish, fish oil and the risk of cardiovascular disease]Tidsskr Nor Laegeforen. 2004;124(2):198-200. Bio-accumulation profiles of chemical contaminants in fish from the lower Willamette River, Portland Harbor, Oregon. Arch Environ Contam Toxicol. 2004;46(1):114-23. Childhood urine mercury excretion: dental amalgam and fish consumption as exposure factors. Environ Res. 2004;94(3):283-90. Is fish consumption safe? J La State Med Soc. 2004;156(1):42, 44-9. Mercury and selenium in whole blood and serum in relation to fish consumption and amalgam fillings in adolescents. J Trace Elem Med Biol. 2003;17 (3):165-70. Ameri-can Society for Circumpolar Health. Comparison of mercury in selected subsistence foods from western Alas-ka. Int J Circumpolar Health. 2003;62(4):448. Survey of total mercury and methylmercury levels in edible fish from the Adriatic Sea. Food Addit Contam. 2003;20(12):1114-9. Hazards of heavy metal contamination.Br Med Bull. 2003;68:167-82.]

Why do we care about the amounts and the ratios of "Omega-3" to "Omega-6" fat?

The reason for the recommendations in suggestions #3-5 above is that increasing the ratio of the omega-3 family of oils relative to the omega-6 family is looking very helpful in **decreasing risk of developing a number of serious health conditions.** It may also slow the progression and/or decrease complications of many medical conditions. It also appears to be a factor in having a healthy pregnancy and in the development of the infant both before and after birth.

There will likely be a lot more fine-tuning of the recommendations coming out for specific types of fat and not just broad classes of fat. For example, new knowledge about certain special types of omega-6 fats is looking interesting as well. An example is one called gamma-linolenic (different from alpha linolenic acid) that appears be quite promising in decreasing nerve damage

(neuropathy) related to diabetes, and in decreasing inflammation. It is also being studied in critically ill patients with very encouraging results, along with other specific types of oil. The best food sources of gamma linolenic acid include nuts, and some leafy greens (like evening primrose oil.) Mother's milk is usually rich in gamma linolenic acid. Although there is still much to learn, there is a rapidly growing body of research being reported in the scientific literature exploring these issues. References of a sampling of the most recent research is shown below:

At Low Doses, a {gamma}-Linolenic Acid-Lipoic Acid Conjugate Is More Effective Than Docosahexaenoic Acid-Enriched Phospholipids in Preventing Neuropathy in Diabetic Rats. J Nutr. 2007 Feb;137(2):368-372. Gamma linolenic acid: an antiinflammatory omega-6 fatty acid. Curr Pharm Biotechnol. 2006 Dec;7(6):531-4. Tumoricidal and anti-angiogenic actions of gamma-linolenic acid and its derivatives. Curr Pharm Biotechnol. 2006 Dec;7(6):457-66. Effects of enteral feeding with eicosapentaenoic acid, gamma-linolenic acid, and antioxidants in mechanically ventilated patients with severe sepsis and septic shock. Crit Care Med. 2006 Sep;34(9):2325-33.

Specific Health/Medical Conditions:

AIDS/ HIV Nutritional treatment for acquired immunodeficiency virus infection using an enterotropic peptide-based formula enriched with n-3 fatty acids: a randomized prospective trial Eur J Clin Nutr. 2001 Dec;55(12):1048-52. Effects of protein-energy malnutrition and human immunodeficiency virus-1 infection on essential fatty acid metabolism in children. Nutrition. 2000 Jun;16(6):447-53. Effects of fish oil on cytokines and immune functions of mice with murine AIDS. J Lipid Res. 1998 Aug;39(8):1677-87.

Alzheimer's Disease A diet enriched with the omega-3 fatty acid docosahexaenoic acid reduces amyloid burden in an aged Alzheimer mouse model. J Neurosci. 2005 Mar 23;25(12):3032-40. Polyunsaturated fatty acids in the central nervous system: evolution of concepts and nutritional implications throughout life. Reprod Nutr Dev. 2004 Nov-Dec;44(6):509-38. Chronic administration of docosahexaenoic acid ameliorates the impairment of spatial cognition learning ability in amyloid beta-infused rats. J Nutr. 2005 Mar;135(3):549-55. Docosahexaenoic acid protects from dendritic pathology in an Alzheimer's disease mouse model.Neuron. 2004 Sep 2;43(5):633-45. Importance of "health foods", EPA and DHA, for preventive medicine. Rinsho Byori. 2004 Mar;52(3):249-53.Low serum cholesteryl ester-docosahexaenoic acid levels in Alzheimer's disease: a case-control study.Br J Nutr. 2003 Apr;89(4):483-9. J Neurosci. 2005 Mar 23;25(12):3032-40. Neuroinflammatory perspectives on the two faces of Alzheimer's disease. J Neural Transm. 2004;111 (3):281-94. Consumption of fish and n-3 fatty acids and risk of incident Alzheimer disease. Arch Neurol. 2003;60(7):940-6. Essential fatty acids and the brain. Can J Psychiatry. 2003;48(3):195-203. Omega-6/omega-3 ratio and brain-related functions. World Rev Nutr Diet.2003;92:37-56. J Neural Transm. 2003;11 (1):95-110. Dietary lipids in the aetiology of Alzheimer's disease: implications for therapy. Drugs Aging. 2003;20(6):399-418. Low serum cholesteryl ester-docosahexaenoic acid levels in Alzheimer's disease: a case-control study. Br J Nutr. 2003;89(4):483-9. The role of diet in cognitive decline. J Neural Transm. 2003;110(1):95-110.

Arthritis Biological basis for the benefit of nutraceutical supplementation in arthritis. Drug Discov Today. 2004 15;9 (4):165-72. Omega-6/omega-3 fatty acids and arthritis. World Rev Nutr Diet.2003;92:152-68. Dietary fatty acids and immune reactions in synovial tissue. Eur J Med Res. 2003;8(8):381-7. A biomarker of n-3 compliance in patients taking fish oil for rheumatoid arthritis. Lipids. 2003;38(4):419-24. N-3 polyunsaturated fatty acids and inflammation: from molecular biology to the clinic. Lipids. 2003;38(4):343-52. Dietary n-3 fats as adjunctive therapy in a prototypic inflamma-tory disease: issues and obstacles for use in rheumatoid arthritis. Prostaglandins Leukot Essent Fatty Acids.2003;68(6):399-405. The role of fish oils in the treatment of rheumatoid arthritis. Drugs.2003;63(9):845-53. Nutritional management of rheumatoid arthritis: a review of the evidence. J Hum Nutr Diet.2003;16(2):97-109. Could n-3 polyunsaturated fatty acids reduce pathological pain by direct actions on the nervous system? Prostaglandins Leukot Essent Fatty Acids.2003;68(3):219-24. Anti-inflammatory effects of a low arachidonic acid diet and fish oil in patients with rheumatoid arthritis. Rheumatol Int. 2003;23(1):27-36.

Asthma Eur Respir J. 2000;16(5):861-5. Cochrane Database Syst Rev. 2000;(4):CD001283.

Bone Health Repletion with (n-3) fatty acids reverses bone structural deficits in (n-3)-deficient rats. J Nutr. 2004 Feb;134(2):388-94.

Cancer Prevention (General) Tumoricidal and anti-angiogenic actions of gamma-linolenic acid and its derivatives. Curr Pharm Biotechnol. 2006 Dec;7(6):457-66.Carcinogenesis. 2003;24(5):919-25. Chin Med J (Engl).203;116(3):453-8; Eur J Cancer. 2002;11 Suppl 2:S1.

Lung Cancer Nutr Cancer.203;45-2:106-7; Nutr Cancer.2002;42(1):18-24; J Nutr.2002;132(7):2069-75.

Breast Cancer Nutr Cancer.2003;45(2)211-217. Dietary flaxseed inhibits human breast cancer growth and metastasis and downregulates expression of insulin-like growth factor and epidermal growth factor receptor. Nutr Cancer. 2002;43(2):187-92. Int J Cancer. 2003;107(2):276-82; J Nutr.203;133(5):1409-14; J Nutr Biochem. 2002;13(12):711-16; Nutr Cancer.2002;43(2):187-92. . Flaxseed inhibits metastasis and decreases extracellular vascular endothelial growth factor in human breast cancer xenografts. Cancer Lett. 2002 8;185(1):31-7

Colon Cancer Effect of an omega-3 fatty acid containing lipid emulsion alone and in combination with 5 fluorouracil (5 FU) on growth of the colon cancer cell line Caco-2.Eur J Nutr. 2003;42(6):324-31. Colon Detect Prev.200327(1):55-6; Cancer Res.203;63(5):972-9; Int Epidemiol.203; 32(2):200 9; Carcinogenesis 2003;4 [Epub ahead of print]. J Nutr 2002;132(11 Suppl):3508S:3512S.

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Adjunct to Chemotherapy in Cancer Treatment Formation and anti-proliferative effect of prostaglandin E3 from eicosapentaenoic acid in human lung cancer cells. J Lipid Res. 2004 Mar 1 [Epub ahead of print]Nutr Cancer. 2002;44(2):176-81; J Control Release.2001;74(1-3):233-6; Clin Cancer Res 2001.7(7):2041-9; Anticancer Res.2001;21 (1A):29-38; Suppression of tumor growth and metastasis by dietary fish oil combined with vitamins E and C and cisplatin. Cancer Chemother Pharmacol. 2001;47(1):34-40. Anticancer Res.1999;19(6C):5583-6.

Cardiovascular Disease (Esp. Heart Disease, Hypertriglyceridemia and Stroke)

Blood omega-3 and trans Fatty acids in middle-aged acute coronary syndrome patients. Am J Cardiol. 2007 Jan 15;99(2):154-8. Greater fish, fruit, and vegetable intakes are related to lower incidence of venous thromboembolism: the Longitudinal Investigation of Thromboembolism Etiology. Circulation. 2007 Jan 16;115(2):188-95. Meta-analysis of the effects of n-3 polyunsaturated fatty acids on haematological and thrombogenic factors in type 2 diabetes. Diabetologia. 2007 Feb;50(2):250-8. Depression and cardiovascular mortality: a role for n-3 fatty acids? Am J Clin Nutr. 2006 Dec;84(6):1513-7. Tumoricidal and anti-angiogenic actions of gamma-linolenic acid and its derivatives. Curr Pharm Biotechnol. 2006 Dec;7(6):457-66. NEJM.2004;350(1) :29-37. Nutr Rev. 2004;62(1):18-27. J Nutr. 2005 Mar;135(3):562-6. Consumption of trans fatty acids is related to plasma biomarkers of inflammation and endothelial dysfunction. n-3 fatty acids and the risk of sudden cardiac death. Emphasis on heart rate variability. Dan Med Bull. 2003;50(4):347-67. Dietary fish oil up-regulates cholesterol 7alpha-hydroxylase mRNA in mouse liverleading to an in-crease in bile acid and cholesterol excretion. FEBS Lett. 2004 cholesterol and paraoxonase levels in patients with familial combined hyperlipidemia. Metabolism. 2004;53(2):153-8. Fish oil increases antioxidant enzyme activities in macrophages and reduces atherosclerotic lesions in apoE-knockout mice. Cardiovasc Res. 2004;61(1):169-76. Fish oil interaction with warfarin. Ann Pharmacother. Microalgal docosahexaenoic acid decreases plasma triacylglycerol in normolipidaemic vegetarians: a randomised trial. Br J Nutr. 2006 Apr;95(4):779-86.2004;38(1):50- 2. Vitamins, supplements, herbal medicines, and arrhythmias. Cardiol Rev. 2004;12(2):73-84. Cardiovasc Res. 2004;61(1):169-76. Flaxseed and cardiovascular risk. Nutr Rev. 2004;62(1):18-27. Flax facts. A grain for good health. Diabetes Self Manag. 2003;20(6):18, 20-2. Dietary flaxseed meal is more protective than soy protein concentrate against Hypertriglyceridemia and steatosis of the liver in an animal model of obesity. J Am Coll Nutr. 2003 ;22(6):494-501.Int J Vitam Nutr Res.2003;73(3):163-70; J Throm Haemost.2003;1(4):690-7; J Women's Health-Larchmt. 2003;12(2):109-14; Int J Clin Pract.2003;57(4):305-14; Circulation.2003;108(7):820-5. Am J Cardiol.2003;91 (7A):1 8E-23E. Circulation.2002;106:289-91.;559(1-3):125-8.]

Chronic Fatigue Syndrome In chronic fatigue syndrome, the decreased levels of omega-3 poly-unsaturated fatty acids are related to lowered serum zinc and defects in T cell activation. Neuro Endocrinol Lett. 2005 Dec;26(6):745-51. Determination of fatty acid levels in erythrocyte membranes of patients with chronic fatigue syndrome. Nutr Neurosci. 2003 Dec;6(6):389-92. Treatment of chronic fatigue syndrome by dietary supplementation with omega-3 fatty acids--a good idea? Med Hypotheses. 2002 Mar;58(3):249-50.

Cystic Fibrosis Bioavailability and safety of a high dose of docosahexaenoic acid triacylglycerol of algal origin in cystic fibrosis patients: a randomized, controlled study. Nutrition. 2006 Jan;22(1):36-46. Biological effects of a dietary omega-3 polyunsaturated fatty acids supplementation in cystic fibrosis patients: a randomized, crossover placebo-controlled trial. Clin Nutr. 2006 Jun;25(3):418-27. Association of cystic fibrosis with abnormalities in fatty acid metabolism. N Engl J Med. 2004;350 (6):560-9. JPEN J Parenter Enteral Nutr. 2003;27(1):52-7. Cochrane Database Syst Rev. 2002;(3):CD002201. J Appl Physiol. 2002;92(5):2169-76. Curr Opin Pulm Med. 2000;6(6):530-2.

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Epilepsy Epilepsia.2002;43(1):103-4; Nutr Health.2002;16(1):51-3; Synapse.2000;37(2):90-4.

Eye Health – Macular Degeneration and others Dietary fatty acids and the 5-year incidence of age-related maculopathy. Arch Ophthalmol. 2006 Jul;124(7):981-6. Cigarette smoking, fish consumption, omega-3 fatty acid intake, and associations with age-related macular degeneration: the US Twin Study of Age-Related Macular Degeneration. Arch Ophthalmol. 2006 Jul;124(7):995-1001. Improvement of visual functions and fundus alterations in early age-related macular degeneration treated with a combination of acetyl-L-carnitine, n-3 fatty acids, & coenzyme Q10. Ophthalmologica.2005;219(3);154-66. Neuroprotectin D1 (NPD1): a DHA-derived mediator that protects brain and retina against cell injury-induced oxidative stress. Brain Pathol. 2005;15(2):159-66. The role of omega-3 long-chain polyunsaturated fatty acids in health and disease of the retina. Prog Retin Eye Res. 2005;24(1):87-138. Hypothesis on the role of nutritional factors in ocular hypertension and glaucoma. J Fr Ophtalmol.2005;28(3):312-6.Effect of docosahexaenoic acid supplementation on retinal function in a patient with autosomal dominant Stargardt-like retinal dystrophy. Br J Ophthalmol. 2004 Feb;88(2):305-6. Biological safety assessment of docosahexaenoic acid supplementation in a randomized clinical trial for X-linked retinitis pigmentosa. Arch Ophthalmol. 2003 Sep;121(9):1269-78. J Nutr Sci Vitaminol (Tokyo). 2003 Jun;49(3: 210-3. Invest Ophthalmol Vis Sci. 2003;44(5):2252-9; Invest Ophthalmol Vis Sci. 2003 44(8): 3685-91; Exp Eye Res. 2003;77(2):167-73.

Inflammatory Diseases (general) n-3 polyunsaturated fatty acids, inflammation, and inflammatory diseases. Am J Clin Nutr. 2006 Jun;83(6 Suppl):1505S-1519S Gamma linolenic acid: an antiinflammatory omega-6 fatty acid. Curr Pharm Biotechnol. 2006 Dec;7(6):531-4. n-3 polyunsaturated fatty acids, inflammation, and inflammatory diseases. Am J Clin Nutr. 2006 Jun;83(6 Suppl):1505S-1519S. Gamma linolenic acid: an antiinflammatory omega-6 fatty acid. Curr Opin Clin Nutr Metab Care.2003;6(4):413-9l; Prostaglandins Leukot Essent Fatty Acids.2003;68(3):219-24; Prostaglandins Leukot Essent Fatty Acids. 2003;69(1):51-9; J Am Col Nutr. 2002;21(6):495-505; Isr Med Assoc J.2002;4(1):34-8.

Inflammatory Bowel Disease – IBD-- Crohn's Disease & Chronic Ulcerative Colitis. Nutr Hosp;2003;18(2):57-64; Lipids.2002;37(10):935-40; Proc Nutr Soc.2002;61(3): 391-5; J Nutr.2002;132(1):11-9.

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Polycystic Ovary Disease and Ovarian Function Trans fatty acid intakes and the risk of ovulatory infertility. Am J Clin Nutr. 2007 Jan;85(1):231-7. J Nutr.2003;133(1):108-6; Lipids. 2002;37(11):1059-65; Srp Arh CelokLek. 2002;130(7-8):251-7.

Pregnancy and Infant Development Issues:

Oils rich in omega-3 fatty acids appear to have important implications in pregnancy and infant nutrition in particular. DHA (a long-chain omega-3 fatty acid) is **a major fat of the brain**, and the research is growing that suggests that providing some pre-formed DHA is advantageous. [Eur J Clin Nutr. 2004;58(3):429-37. Pediatrics 2003;111(1):e39-44; Arch Dis Child Fetal Neonatal Ed.2003;88(5):F383-F390.] DHA is known to be essential for **retinal development** in infants [Invest 44(8):3685-91; Ophthalmol Vis Sci.2003;Invest Ophthalmol Vis Sci.2003;44(8):3685-9.] It has also been reported that maternal alcohol intake can alter fatty acid transport by the human placenta, decreasing fetal availability of polyunsaturated fats in general and of DHA especially. (Br J Nutr. 2002; 87(3):247-52.) It may be that this decreased DHA transport is one of the (many) mechanisms of **FAS (Fetal Alcohol Syndrome.)**

Omega-3 fats are also associated with **decreased risk of premature delivery**. As premature delivery is the most common cause of low infant birth weight, and infant morbidity and mortality, this is a very important observation. [J Nutr.2003;133(5 Suppl 2): 1606S-1625S. Exp Biol Med (Maywood). 2001;(226(6):498-506; BMJ.2002;324(7335):447; Obstet Gynecol Serv.2001;56(5 Suppl 1):S1-S13; Pediatrics. 2001 Aug;108(2):359-71; Obstet Gynecol Surv. 2001;56(5 Suppl 1):S1-13; Pediatr Clin North Am.2001;48(1):173-88; BJOG.2000;107(3):382-95.]

There is growing interest in the potential role of maternal supplementation of anti-inflammatory n-3 polyunsaturated fattyacids (n-3 PUFAs) in the prevention of allergic disease. [J Allergy Clin Immunol. 2003 Dec;112(6):1178-84.] For more information on this topic please see “Aunt Cathy’s Guide to Nutrition: A Top Ten Nutrtion Plan for Optimizing Pregnancy.”

Nutrition in brain development and aging: role of essential fatty acids. Nutr Rev. 2006 May;64(5 Pt 2):S24-33; discussion S72-91. Nutrition and theory of mind--The role of polyunsaturated fatty acids (PUFA) in the development of theory of mind. Prostaglandins Leukot Essent Fatty Acids. 2006 Jul;75(1):33-41. Omega 6 to omega 3 fatty acid imbalance early in life leads to persistent reductions in DHA levels in glycerophospholipids in rat hypothalamus even after long-term omega 3 fatty acid repletion. Maternal dietary (n-3) fatty acid deficiency alters neurogenesis in the embryonic rat brain. J Nutr. 2006 Jun;136(6):1570-5. Fatty acids differentially affect serotonin receptor and transporter binding in the rat brain. Neuroscience. 2006;139(4):1397-403. Fatty acids differentially affect serotonin receptor and transporter binding in the rat brain. Neuroscience. 2006;139(4):1397-403. Reduced brain DHA content after a single reproductive cycle in female rats fed a diet deficient in N-3 polyunsaturated fatty acids. Biol Psychiatry. 2006 Nov 1;60(9):987-90. Role of docosahexaenoic acid in neuronal plasma membranes. Sci STKE. 2006 Feb 7;2006(321):pe6. Docosahexaenoic acid facilitates cell maturation and beta-adrenergic transmission in astrocytes. J Lipid Res. 2006 Mar;47(3):571-81. Overexpression of dopamine receptor genes and their products in the postnatal rat brain following maternal n-3 fatty acid dietary deficiency. J Neurochem. 2005 Dec;95(6):1550-62. A randomized trial of docosahexaenoic acid supplementation during the third trimester of pregnancy. Obstet Gynecol. 2003 Mar;101(3):469-79

What is a Good Ratio of Omega-3 to Omega-6 Fatty Acids to Aim For?

Most Americans eat about ten grams of omega-6 fat for every one gram of omega-3. That is, the ratio is ten to one. Some estimates are even higher. **We should try to change that ratio to four-to-one, and if we have an inflammatory disease, two-to-one might even be better.** Corn oil is almost all omega-6, so it is not the best choice. Compared with omega-3 fats, the omega-6 fats tend to increase inflammatory responses. If you buy a fish oil supplement, look for the words "EPA and DHA" on the label -- these are the "good guy" omega-3 fats that you are trying to get. (I remember this by thinking of EPA as "Environmental Protection Agency" since it protects your personal internal environment.)

A report on EPA-DHA (NOT on cod-liver oil, which is different in a number of ways) supplements available in the U.S. appeared in **Consumer Reports** (2003Jul;68(7):30-2.) They evaluated the **safety** of products on the market (e.g. related to mercury concerns, etc.), the **actual content** of each product, and the **price**. The good news is that they found all to be safe, and all products contained what the label said was in there. However the **price** per 300 mg of supplemental fish oil ranged from 6 to 60 cents each! Expensive items provided no additional benefit. The cheapest are found at bulk-sales stores like Sam's Club or Costco, etc. (in BIG bottles.) Most pharmacies carry them in smaller bottles.

Alpha linolenic acid is the form of omega-3 fat found in plants. Flax, canola and walnut oil are the most generous sources. Usually we can use it to make the EPA and DHA we need, but many people clearly benefit from getting at least some EPA and DHA "ready-made," (i.e. in fish and fish oil supplements.) For example, some people may have difficulty making adequate EPA out of the omega 3 fats in plants. Another group of people at particular risk of cardiovascular disease was identified who have a different genetic trait for which providing EPA may be especially helpful. They have a variant 5-lipoxygenase genotype affecting leukotriene production and inflammation. (NEJM.2004;350(1):29-37; Nutr Rev. 2004 Jan;62(1):18-27.)

Some guidelines are now available: A qualified health claim for fish oil supplements with EPA and DHA in capsule form has been approved by the FDA. The supplements should be used with a physician's knowledge and approval, as certain aspects of the use of high doses of fish oil can increase bleeding problems among people taking certain medications to decrease risk of clots. These include anticoagulant and antiplatelet medications like Coumadin. Supplements that provide about a gram (1000 mg) of omega-3 fat daily can benefit persons with cardiovascular disease. Higher dose (2–4 grams, or 2000-4000 mg) intakes appear to greatly improve high triglyceride levels in particular. The higher doses (over 3 grams daily) should be taken only with physician approval. (n-3 Fatty Acids: Recommendations for Therapeutics and Prevention. Proceedings of a symposium, New York, New York, USA, May 21, 2005. Am J Clin Nutr. 2006 Jun;83(6 Suppl):1451S-1538S. AHA Nutrition Committee. Fish consumption, fish oil, omega-3 fatty acids, and cardiovascular disease. Circulation 2002;106:2747-2757.)

The chart on the next page shows the families of oils and the names of the fats in each family. To help me remember them, I gave each "family" a last name that reminds me of some of the major food sources of each. The omega-3 family is the "Fishers," the omega-6 family's last name is "Cornelius," and the monounsaturated fats are the "Olivetti" family. The dotted line is the marker of the forms of these fats found in plants, and the forms that are found only in "critters" like fish and animals, including people. The critters themselves can usually make the EPA, DHA and ARA out of the plant forms that they eat, and they also take them in by eating other critters.

Why we care about this:

Prostaglandins, thromboxanes, prostacyclins, and leukotrienes are made from 20 carbon polyunsaturated fatty acids (EPA and ARA). Thromboxanes made from ARA are much more aggregatory (promoting of blood clots) than those made of EPA. Prostaglandins made of ARA are much more inflammatory than those made of EPA. **Decreasing the ratio of omega 6 to omega 3 fatty acids in the diet decreases the likelihood of forming blood clots, and decreases inflammation.** This is particularly important in cardiovascular health, in diabetes, and in autoimmune diseases such as MS, inflammatory bowel disease, lupus and arthritis. A typical omega 6:omega 3 ratio in the US is often as high as 10:1. A suggested ratio goal for healthy people: 4:1. A ratio of 2:1 has been suggested for people with inappropriately inflammatory or aggregatory conditions.

The Unsaturated Fat Families:

Number of Carbons: **Number of Double Bonds**	**Omega 3** "The **Fish**er family"	**Omega 6** "The **Corn**elius family	**Omega 9** "The **Olive**tti family" ("Monounsaturated")
		Linoleic* 18:2 ↓	(plants)
18 carbons	Alpha Linolenic* 18:3 ↓	Gamma Linolenic 18:3 ↓	Oleic 18:1 ↓
20 carbons	EPA** 20:5 ↓	Arachidonic (ARA) 20:4	(critters)
22 carbons	DHA*** 22:6		

* **Essential fatty acids** ***linoleic = 18:2** ***alpha linolenic = 18:3**

** **Eicosapentaenoic acid**
Eicosa: 20 (carbons) Penta :with 5 Enoic: double bonds

*** **Docosahexaenoic acid** (an important component of the brain)
Docosa: 22 (carbons) Hexa: with 6 Enoic: double bonds

(New research issue: Is docosahexaenoic acid (DHA) essential? Lessons from DHA status regulation, our ancient diet, epidemiology and randomized controlled trials. J Nutr. 2004 Jan;134(1):183-6)

The chart on the next page shows the plant and animal food and oil sources for omega-3 fats in descending order. The animal sources (including fish) are on the right, and plant sources are on the left. It is interesting to note that olive oil and peanut oil are not very generous sources of omega-3 fat. Their contribution to heart health (for example, as a part of the "Mediterranean Diet") appears to be due to their **displacement** of other, less-healthful fats in the diet, such as the omega-6 fats and saturated fats. Displacing some of the dietary omega-6 fats is another way to **decrease the ratio** omega-6 toomega-3 fat.

Omega 3 Fatty Acids in Foods

Plant Forms:

Linolenic Acid (18:3)

Mg omega-3 fatty acids per tablespoon of food (unless otherwise noted)

Linseed oil (flax)	7300
Rapeseed (Canola) Oil	1500
Walnuts, English, chopped	1440
Walnut Oil	1400
Wheat germ	900
Soybean oil	900
Soybean Sprouts, cooked 1 oz	600
Hydrogenated Soybean Oil	300
Olive Oil	100
Safflower Oil	100
Sunflower Oil	100
Corn Oil	100
Peanut Oil	0
Palm Oil	0
Palm Kernel Oil	0
Cottonseed Oil	0
Coconut Oil	0

Source:
Omega 3 values from "Provisional Table on Content of Omega-3 Fatty Acids and Other Fat Components in Selected Foods" USDA Human Nutrition Information Service 1986, and Agriculture Handbook No. 8-4
US Dept. of Agriculture Science and Education Administration

New Source: **DHA produced by the use of microorganisms.** Biotechnological production and applications of the omega-3 polyunsaturated fatty acid docosahexaenoic acid. Appl Microbiol Biotechnol. 2004 Jan 22

Animal Forms:

EPA and DHA (20:5 and 22:6)
(Eicosapentaenoic Acid and Docosahexaenoic Acid)

Seafood portion in ounces to equal 300 mg of omega-3 fatty acids (uncooked weight)

Fish oil 300 mg capsule	1 capsule
Mackerel, Atlantic	0.4
Trout, Lake	0.5
Herring, Atlantic	0.7
Sardines	0.7
Anchovies, European	0.8
Salmon, Pink	1.0
Tuna, white	1.3
Bass, striped	1.3
Trout, Brook	1.8
Tuna, Light	2.1
Cod	3.5
Crab, king	3.5
Shrimp	5.3
Flounder	5.3
Haddock	5.3
Lobster	5.3
Scallops	5.3
Snapper, Red	5.3
Swordfish	5.3
Sole	10.5

MeritCare Health System's

Aunt Cathy's Guide to Nutrition:

MAGNESIUM

Aunt Cathy 4/2007
Cathy Breedon PhD, RD, CSP, FADA
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Short Version with Minimal References Included

This shorter version includes only a few of the many references from the scientific literature. If you are interested in seeing the rest of the references, you can access a version on line that includes this information. Go to www.meritcare.com and type Cathy Breedon in the search box. A page will come up that has a box labeled "Cathy Breedon's Handouts" and you can check the one they have labeled "Guide to Nutrition: Magnesium (PDF)" Other topics are also available at this site**. For this cardiovascular health conference, additional reference material will be provided separately about this particular aspect of magnesium nutrition.**

RDA: Adult women 320; men 420mg
Pregnancy 350-400 mg
Lactation 320-360 mg

1) This mineral plays a role in over 300 functions in the body, including energy production, nervous system activity, and bone flexibility.

2) Most American adults take in less that 2/3 of the RDA.

3) Some estimates indicate that as many as a third of hospitalized patients have a low magnesium level in their blood that can complicate their care. Poor magnesium status upon entering a hospital is a predictor of a less favorable outcome. Blood magnesium level does not necessarily reflect magnesium adequacy, however. Usually it just indicates that a person's kidneys are on the job, since the blood Mg level is regulated by the kidney. So if one's blood level is low, it may reflect inadequate intake or excessive losses (and so this is a very important laboratory finding.) However, a normal blood level tells us very little about the adequacy of magnesium inside the body's cells, where most of the magnesium-dependent work is trying to be done. In other words, the best way to know if people's intake of magnesium is appropriate is to obtain a careful history of their usual intake from foods and supplements. This is rarely done.

4) Low magnesium status is associated with a number of adverse health conditions. However, as is the case for most minerals, excessive intake from high-dose supplements is not safe.

A Brief Overview of Associations of Magnesium Status with Adverse Health Conditions:

Diabetes:

High blood sugar contributes to **magnesium loss** in the urine and at the same time poor magnesium status can **increase insulin resistance** because magnesium is required by the insulin receptors on the cells. Low magnesium intake may also contribute to the **development** of diabetes, heart disease and stroke, and to certain complications of diabetes such as retinopathy and neuropathy. Many studies have shown that people with diabetes often have poor magnesium status. Improved blood sugar control is associated with eating a "high fiber diet, " which also provides a better intake of magnesium and chromium, both of which play very important roles in blood sugar and lipid metabolism.

For example, recently researchers at Harvard University published the results of a prospective study at of almost 84,000 women who were followed for 16 years. It was found **that those who ate nuts or peanut butter four times a week or more had 25% less likelihood of developing Type II diabetes** (the adult type) than was found for women who ate these foods rarely or never. Nuts and peanut butter are especially rich in magnesium, chromium, vitamin E, monounsaturated fat and omega-3 polyunsaturated fats. All of these nutrients have the potential to have played a protective role in this study. Later the data was analyzed differently, it was found that **the same pattern existed when the highest and lowest magnesium intake groups were compared**. Magnesium inadequacy also is being implicated as a contributor to the development of Type II diabetes in young people that is evolving from the epidemic of childhood obesity .

Cardiovascular Disease and Hypertension:

Abnormal magnesium status is common in patients with cardiovascular diseases for a number of reasons, including poor dietary intake or excessive losses due to use of diuretics or diabetes. Dietary magnesium inadequacy is an independent risk factor in predicting the development of hypertension and cardiovascular disease. Some of the benefits of high fiber diets, legumes (especially peanuts) and nut consumption in decreasing cardiovascular risk are likely due in part to the magnesium content. (Please see the newest references provided separately)

Osteoporosis and Bone Health:

Healthy bone production relies on the implantation of calcium into a flexible core called the bone "matrix." Magnesium is crucial for the development of the bone matrix, and so **inadequacy can increase the fragility of bone** (because it is less flexible) and it can impair recovery from bone injury.

It is also important to note that calcium and magnesium also interact in other areas of the body, such as nervous system function, blood pressure control and blood clotting, so maintaining an appropriate ratio is extremely important. For example, there is concern that excessively generous calcium supplementation without attention to the calcium: magnesium ratio may increase risk of thrombosis and stroke. With so much calcium fortification and supplementation taking place, we cannot afford to ignore the fact that many Americans have a poor magnesium intake and/or high magnesium losses.

Pregnancy:

Some researchers feel that prenatal magnesium adequacy has a higher priority than even iron supplementation because of the over 300 enzyme systems in the body that depend on magnesium to function properly. Several measures of pregnancy outcome, such as **higher frequency of spontaneous abortions (miscarriage), fetal growth retardation, birth defects, maternal hospitalizations, preterm delivery, SIDS and referrals to NICUs** have been found to be associated with poor magnesium status in pregnancy. [These issues are related to general nutrition and are separate from issues related to the acute therapeutic i.v. magnesium sometimes used in the treatment of pre-eclampsia or premature labor.]

Other studies have shown a benefit of assuring magnesium adequacy (i.e. providing the RDA level of magnesium) in the reduction of **leg cramps** in pregnancy. **Pregnant women with diabetes** need special attention to adequacy of magnesium intake because of the potential for increased losses and the common finding of poor magnesium status among people with diabetes in particular. In addition, inadequacy of magnesium is a risk factor for the **development of gestational diabetes** as well as Type II diabetes.

Migraine Headaches:

For some migraine sufferers, **assuring adequacy** of magnesium intake resolves migraine problems. For others, it decreases the frequency or intensity of the headaches. So, while Mg status is certainly not the only factor involved in the development of migraines, this intervention can be helpful, and it is safe and inexpensive, so many experts in headache treatment regard assuring magnesium adequacy as a primary intervention.

Premenstrual Syndrome (PMS):

Providing magnesium at the RDA level has been shown to improve “affect” (mood or emotional well-being), and certain tissues of women suffering from PMS have been shown to be low in magnesium. Brain levels of the neurotransmitter serotonin appear to be significantly involved in PMS, and medications that adjust serotonin levels are now being used. Assuring adequacy of magnesium may be a factor (both with and without other medication) because it also is required for the production and metabolism of serotonin (and all neurotransmitter metabolism.)

Cancer:

In 2005 a population-based prospective study of 61,433 women suggested that a high magnesium intake may reduce the occurrence of **colorectal cancer**. Animal studies have also suggested that a higher dietary intake of magnesium is associated with decreased risk of colon cancer, possibly related to an effect of the magnesium-containing substance called chlorophyll protecting against cancer-promoting properties of a structurally similar substance in red meat called heme (or "haem" in the UK.) In addition, in 2004 it was reported that a lower magnesium level in drinking water was associated with risk of death from **ovarian cancer**.

Kidneys, stone forming, and other renal issues:

Low magnesium intake has a role in the development of kidney stones, and the kidney has an important role in regulating magnesium in the blood.

Miscellaneous:

Magnesium adequacy has been found to be a factor in the development and/or management of many chronic conditions, such as **asthma**, certain **thyroid** conditions, **alcoholism**, **pancreatitis**, **hearing loss**, and possibly **Tourette's Syndrome, Raynaud's phenomenon, pain management**, corneal disease, skin problems, attempts to quit **smoking**, and certain **hyperexcitable states.**

Magnesium Losses and Safety Issues:

Conditions like **chronic diarrhea, high blood sugar, or the regular use of certain drugs** (such as thiazide diuretics) cause magnesium loss. As a rule, drugs for which patients are advised to eat a high potassium diet or to take potassium supplements are also likely to cause loss of magnesium. This problem is often unrecognized, however, and because of an interaction between magnesium and potassium, the failure to correct magnesium losses along with potassium losses further compromises the body's ability to achieve normal potassium status in the cells. As is the case with potassium, **most vitamin/mineral supplements contain little magnesium or none at all**. And also like potassium, there may be **a need to take in less when one has certain kidney problems.**

Excessive intake from supplements or magnesium-containing medications can also cause problems, so never give nutritional supplements of magnesium above the level described above unless prescribed by a doctor. It is also useful to know that magnesium oxide, chloride and diglycinate are the kinds of magnesium that are usually used as a supplement . . . magnesium sulfate (Epsom salts) and hydroxide ("milk of magnesia") are less well absorbed and more likely to cause diarrhea instead (which is why they are used to treat constipation . . . in fact, magnesium citrate is often used as a pre-surgical bowel-cleaning product!) There are a number of magnesium-containing medications, like some over-the-counter antacid products. Check with a pharmacist about magnesium in specific products.

Food Sources of Magnesium:

Food sources are the **best way to safely assure adequacy**, with the added benefit of the other nutrients they provide and the pleasure derived from eating them. Unlike supplement sources, dietary sources of magnesium do not contribute to diarrhea, and there is not a concern about potential overdose. Only individuals with renal failure or another serious medical condition may be advised by a physician to limit intake of dietary magnesium.

As can be seen below, the best sources or magnesium are also foods recommended as healthy choices by the American Dietetic Association, and by many professional health associations concerned with cardiovascular health, diabetes and cancer. And although the nuts and peanut butter do contribute fat and calories, they can easily be included as a part of a healthy diet when used in place of other high calorie or high fat foods. As an added bonus, the form of fat in these foods is rich in monounsaturated fat and omega-3 fatty acids. They are low in saturated fat and trans fatty acids, have no cholesterol, and compared with other forms of fat, they are generally found to be protective against heart disease, diabetes and cancer.

Some of the Best Dietary Sources of Magnesium:

Magnesium (mg per 1/2 cup)

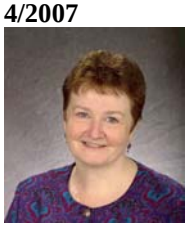
500 mg or more	**Peanuts and Peanut butter**
100-300mg	**Wheat germ***, **Bran cereals***, **Wild rice** **Lentils, Split peas, Tofu,** **Cashews, Almonds**
	*Note that refining grains removes most of the magnesium and it is **not** added back as iron is when grain is "enriched." The phytate content of the grain is also a factor in the availability of dietary magnesium.
25-90 mg	**Fortified breakfast cereals, Oatmeal,** **Miso, Spinach,** **Milk, Yogurt, Fish,** **Brewer's yeast** (80 mg/Tblsp), **Cocoa powder** (25 mg/Tblsp)

Meritcare Medical Center

4/2007

Aunt Cathy's Guide to

Vitamin D: It's not just for bones anymore!



Aunt Cathy
Cathy Breedon PhD, RD, CSP, FADA
Clinical Nutrition Specialist
MeritCare Medical Center Fargo, ND
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Calcium absorption relies on vitamin D adequacy

It is well known that Vitamin D is important for the absorption of calcium. To be used by the body, calcium must be absorbed from foods or supplements through the lining of the intestine. Vitamin D is necessary for calcium absorption to occur, but the vitamin D that helps with calcium absorption is not that in the current meal or supplement . . . it is the vitamin D already in your body that does the job. That is, vitamin D can be thought of as helping to "pull" calcium into the body from the inside rather than as "pushing" it in from the outside. For this reason, the vitamin D does not have to be present as a part of the calcium supplement in order to work. If you have sufficient vitamin D in your body from other sources (from exposure to the sun, from a vitamin pill, from milk, etc.), it may be unnecessary to have additional vitamin D in the calcium pill. However, for reasons to be described later, for many people needing a calcium supplement, the products that also provide additional vitamin D will be advantageous for other reasons. [In Brief: Vitamin D shortfalls casting wider shadow. Harv Health Lett. **2004**;29(5):7. Macronutrients: vitamin D. Dis Mon. **2004**;50(2):59-68. Vitamin D in preventive medicine: are we ignoring the evidence? Br J Nutr. **2003**;89(5):552-7. Vitamin D: A millenium perspective. J Cell Biochem. **2003**;88(2):296-307. Hypovitaminosis D: a major worldwide public health problem. Presse Med. **2001**;30(13):653-8.]

Vitamin D is not just for bones any more!

Vitamin D is important for preventing rickets (a bone deformity disease) in infants and children, and breastfed infants in particular should receive a standard vitamin D drop. In spite of vitamin D's availability from the effects of sunlight on skin, it has recently been recognized that **many people do not obtain sufficient vitamin D, and their blood vitamin D levels are low**. This includes nursing mothers, of course. However, regardless of the mother's own vitamin D status, human milk does not provide adequate amounts of this critical vitamin. This may reflect the fact that when people were "invented," no one lived in North Dakota -- babies crawled about in the sun down by the equator and made their own vitamin D. Rickets has been documented in breast-fed infants of all races in all climates. Dark-skinned infants are at special risk. **Interesting ly, the classic presentation of vitamin D deficiency (deformity of the leg bones, the ribs and the skull) are not always present.** In some cases, vitamin D deficiency in infants and children has been detected following seizures or muscle pain without visible bone damage. [Nutritional rickets in childhood: analysis of 62 cases. Med Clin (Barc). 2003;121(1):23-7. Symptomatic rickets in adolescence. Arch Dis Child. 2001;84 (6):501-3. A baby with bulging anterior fontanelle. Lancet. 2000;356(9224):132. Vitamin D deficiency rickets in breast-fed infants presenting with hypocalcaemic seizures. Acta Paediatr. 1995;84(8):9412.]

Vitamin D deficiency can also occur without any symptoms. If symptoms are present, it indicates severe deficiency. [Tuberculosis and vitamin D deficiency. J Assoc Physicians India. 2002;50:554-8.] Serum calcium and phosphorus values do not often predict the existence of deficiency. Because of the other serious effects of deficiency (described later), there is a philosophical problem: waiting until a child exhibits overt bone damage before assuring that they are receiving adequate vitamin D is surely not the best model of preventive medicine.

Current Recommendation for Infants, Children and Adolescents. In 2003, the American Academy of Pediatrics issued the following recommendation regarding vitamin D supplement ation in infants. "Rickets in infants attributable to inadequate vitamin D intake and decreased exposure to sunlight continues to be reported in the United States. **It is recommended that all infants, including those who are exclusively breastfed, have a minimum intake of 200 IU of vitamin D per day beginning during the first 2 months of life. In addition, it is recommended that an intake of 200 IU of vitamin D per day be continued throughout childhood and adolescence,** because adequate sunlight exposure is not easily determined for a given individual. These new vitamin D intake guidelines for healthy infants and children are based on the Recom mendations of the National Academy of Sciences." [Pediatrics 2003 Apr;111(4 Part1):908-10.] However, not all health care providers have received the message. For example, of 155 pediatric health care providers surveyed in Las Vegas, Nevada, 52.3% did not recommend vitamin D for exclusively breastfed babies.[Pediatrics 2003 Apr;111(4 Part1):908-10. Practices of vitamin D recommendation in Las Vegas, Nevada. J Hum Lact. **2004**;20(1):56-61. Pediatrician patterns of prescribing vitamin supplementation for infants: do they contribute to rickets? Pediatrics. **2004**;113(1 Pt 1):179-80. Vitamin D and bone health in early life. Proc Nutr Soc. **2003**;62(4):823-8.]

Receptors for calcitriol (1,25 dihydroxy vitamin D) have been found to be present in over 30 different tissues.

New research is also documenting potentially important roles for vitamin D in the prevention or progression of conditions such as:

Arthritis: osteo and rheumatoid

Cancer (prostate, colon, breast and pancreas)

Dermatology

Diabetes (type I and type II)

Heart Disease

Inflammatory Bowel Disease

Lupus and Fibromyalgia

Multiple Sclerosis (MS).

Myopathy and Sarcopenia (muscle damage and weakness)

Osteoporosis

Pregnancy Issues:
Impaired fetal development, prenatal programming of adult disease (Fetal Origins Hypothesis), high blood pressure(PIH), schizophrenia.

Tuberculosis

The references from each of these areas are so voluminous that I moved them all to the end and filed them by health condition.

Assuring adequacy may well have far-reaching benefits. **Conversely, failure to provide adequate amounts may have a heavier price tag than was previously thought.** There is evidence that vitamin D intake during childhood and adolescence may be especially important in relation to the development many of these chronic conditions. For example, poor vitamin D status in young children is now known to be a clear risk factor for the development of Type I diabetes in children around the world.

Poor vitamin D status, especially around round the time of adolescence is a known risk factor in the development of Multiple Sclerosis (MS), a condition that is much more common in the northern latitudes in the US than in the sunnier south. In fact, in addition to it's well recognized title of being the **"Rickets Belt,"** the northern third of the United States is also well known to be the "**MS Belt**" and the **"Type I Diabetes Belt**". For this reason, concern about vitamin D status needs to extend throughout the lifecycle. Vitamin D inadequacy is common in the U.S. among all age groups, and the consequences of failing to assure adequacy are extremely serious. [In Brief: *Journal of the American Academy of Dermatology* 2005;52(5): 868. Vitamin D shortfalls casting wider shadow. Harv Health Lett. **2004**;29(5):7. Macronutrients: vitamin D. Dis Mon. **2004**;50(2):59-68. Vitamin D in preventive medicine: are we ignoring the evidence? Br J Nutr. **2003**;89(5):552-7. Pediatrics **2003**;111(4 Part1):908-10. Vitamin D: A millenium perspective. J Cell Biochem. **2003**;88(2):296-307. Hypovitaminosis D: a major worldwide public health problem. Presse Med. **2001**;30(13):653-8.]

Recently researchers at the Mayo Clinic in Rochester MN reported that vitamin D inadequacy is an important factor in **persistent nonspecific musculoskeletal pain**. Interestingly, they found significant vitamin D inadequacy in people usually considered to be low risk for vitamin D deficiency. Their recommendation:"…screening all outpatients with such pain for hypo-vitaminosis D should be standard practice in clinical care." [Prevalence of severe hypovitaminosis D in patients with persistent, nonspecific musculo-skeletal pain. Mayo Clin Proc. **2003**;78(12):1463-70.]

How much vitamin D?

In northern latitudes, vitamin D deficiency used to result in an epidemic of rickets, and as noted earlier, that area of the country was called the **"Rickets Belt."** Vitamin D was added to milk in an effort to solve this serious health problem. Studies in Boston the late 1990's showed that **1.5-2 times the RDA for vitamin D may be required to maintain normal blood levels of vitamin D in that region** because of the inefficiency of vitamin D production in the skin during the winter months.

Other people produce little vitamin D in their skin because they have dark skin, or they are clothed so that that little skin is exposed to light. In a recent report, the researchers at Boston University indicated that "The recommended adequate intakes for vitamin D are inadequate, and, in the absence of exposure to sunlight, a minimum of 1000 IU vitamin D/d is required to maintain a healthy concentration of 25(OH)D in the blood." [Am J Clin Nutr. **2004;**79(3): 362-71.] Serum 25 hydroxy vitamin D levels less than 9 ng/ml indicates deficiency. [Vitamin D administration to tuberculous children and its value. Boll Chim Farm. **1998**;137(5):157-64.] The oral dose necessary to achieve adequate serum

25(OH)D levels is probably much higher than the current recommendations of 5-15 microg/d. Serum levels of 25(OH)D are the best indicator to assess vitamin D deficiency, insufficiency, hypovitaminosis, adequacy, and toxicity. European children and young adults often have circulating 25(OH)D levels in the insufficiency range during wintertime. . [Vitamin D in preventive medicine: are we ignoring the evidence? Br J Nutr. **2003**;89(5):552-7.] In another study, an inverse association was found for vitamin D intake greater than 645 IU/d and risk for colonic cancer in asymptomatic individuals. [JAMA. **2003**;290(22):2959-67.]

When a person is already seriously deficient, other levels may be advised. "The treatment of hypovitaminosis D is simple . . . with administration of vitamin D supplements (calciferol, at least 800 IU). Severe cases may demand initial parenteral administration of vitamin D (repeated injections of 300,000 IU 2-3 times with monthly intervals). More potent analogues are rarely needed. One should aim at achieving S-25(OH)D values in the range 50-100 nmol/l." [Vitamin D deficiency and aging: implications for general health and osteoporosis. Biogerontology. **2002**;3(1-2):73-7.]

The amount of vitamin D that an individual actually produces may be much less than the amount assumed to be available from skin production for the "average" American. For Northern populations, obtaining an adequate intake from food could require 6-8 cups of fortified milk daily
if a supplement were not used. This is a clearly an unrealistic amount. Drinking this much milk would also displace other foods, likely leading to a suboptimal intake of other nutrients.

Vitamin D Content of Foods (Best Sources):

Food:	**Serving Size:**	**Average iu of Vitamin D**
Salmon	3 oz	340
Tuna	3 oz	150
Shrimp	3 oz	127
Vitamin D fortified milk (any kind)	1 cup	100
Liver (beef or chicken)	3 oz	42
Fortified cereals	1 cup	many have 40-60 (check label)
Egg Yolk	1	27
Newly fortified with vitamin D:		
Some brands of yogurt	1 cup	100
Some brands of calcium-fortified orange juice	1 cup	100

For the person who does not drink milk (or drinks very little) the risk of inadequacy is much greater. There are few natural food sources besides liver (see below). Vitamin D is added to milk (i.e. milk is not naturally rich in vitamin D), so **cheese and ice cream are not good**

sources of vitamin D even though they contribute protein and calcium. In 2002, **some yogurt producers began to add vitamin D to some (but not all or even most) of their yogurt products.** Homemade yogurt using fortified milk contains the same amount of vitamin D as is in the milk. Milk directly "from the farm" is a poor source of vitamin D because it has not been added yet. This issue is sometimes overlooked in farm families. Recently, experimental feeding of extra vitamin D to chickens was shown to increase the amount in egg yolk, although this is not yet being done. [Effect of vitamin D2- and D3-enriched diets on egg vitamin D content, production, and bird condition during an entire production period. Poult Sci. **2004**;83(3):433-40.]

Vitamin D intake may be adequate among milk-drinkers who rely on oral vitamin D intake, but it will not be adequate if vitamin D-fortified milk is not consumed in generous amounts. The same amount of vitamin D is added to fat free milk, low fat milk, whole milk and chocolate milk: about 100 iu/cup milk; the RDA = 400 iu or 10 mcg.) Most adult multivitamins and those for children over age 4 years provide 400 iu of vitamin D. **For this reason the simple expedient of taking a daily multivitamin/mineral provides a very good start. Then the vitamin D-rich foods shown in the table above or a calcium supplement with vitamin D, should be used as needed to reach the suggested 600-1000 iu "up north."**

Some **soy beverages are now fortified** like milk, but check the label to be sure. Remember that (as with milk) a significant amount must be consumed even to meet the RDA. In fact, more would be needed than the total number of servings from the entire dairy group (which includes cheese, etc.) suggested by the "Food Guide Pyramid" [Vitamin D deficiency rickets due to soybean milk. J Paediatr Child Health. **2004**;40(3):154-5.] Also note that many **foods that are fortified with calcium (such as certain brands of orange juice and bread) are usually not fortified with vitamin D**. However, some of the companies that produces a calcium-fortified version of their orange juice now also fortifies it with vitamin D. For now, most such products continue to contain no vitamin D because orange juice is not naturally a source of vitamin D. [Development and assessment of a short instrument for assessing dietary intakes of calcium & vitamin D. J Am Pharm Assoc (Wash DC). **2003**;43(6):685-93.]

The New 2005 Pyramid and the Problem of Vitamin D Inadequacy

As described above, the (now "old") Food Guide Pyramid did not address vitamin D at all. On that pyramid, people were encouraged to eat 2-3 servings of foods "from the dairy group" (unrelated to the vitamin D content.) This advice would result in an intake of practically no vitamin D from this group (if all cheese, ice cream or unfortified yogurt were chosen) to 300 iu at the most (assuming 3 cups of fortified milk or yogurt were the products chosen.) One reason for this was the fact that the Food Guide Pyramid was published at just about the same time that the vitamin D issues began to be raised in the professional literature.

In light of the avalanche of research on the frequency and seriousness of the problem of vitamin D inadequacy since then, one would have hoped that this would be addressed in the new version**. Unfortunately the new pyramid that came out in 2005 does not address this problem either.** For example, the sample 7-day 2000 Kcal menus provided on the website add up to an average intake of 320 iu of vitamin D per day, but **only** if milk and fortified yogurt are included. Without milk (but including cheese, etc,) the average drops to 95 iu per day. In addition, in the seven-day menu, salmon and tuna were both included. **Without the fish on the**

menu, the "no-milk" vitamin D content drops to less than 20 iu/day, even assuming that the cereals chosen were fortified.) (http://www.mypyramid.gov/downloads/sample_menu.pdf) The sample menu says "Averaged over a week, this seven day menu provides all of the recommended amounts of nutrients and food from each food group." **To see how this claim can be made, it is worth noting that on the list of nutrients by which they judge a healthy diet, they have completely left out vitamins D and K in their analysis!**

And while fish consumption is generally encouraged because of the omega-3 fats, many people avoid eating fish because of concerns about toxins like mercury, or allergy or simple dislike. Salmon is the most generous source of vitamin D (see the Table on page 4) but it currently has some safety problems and it is expensive. For example, a recent report indicates that "Consumption of farmed salmon at relatively low frequencies results in elevated exposure to dioxins and dioxin-like compounds with commensurate elevation in estimates of health risk." [e.g. Mercury in commercial fish: optimizing individual choices to reduce risk. Environ Health Perspect. 2005 Mar;113(3):266-71. More references at the end of this paper.]

Tuna is one of the most easily available fish, but in some studies tuna had the highest mercury value. The mean level of mercury in white tuna (mean 0.407 ppm) was significantly higher than the mean value of 0.17 ppm currently used by the U.S. Food and Drug Administration (FDA) in its risk assessment and public information. The current Canadian advisory to children and women of childbearing age is to limit consumption of fresh and frozen tuna, swordfish and shark to no more than one meal per month. **In any case, counting on a generous salmon or tuna intake to assure vitamin D adequacy is quite unrealistic.** Information about levels of methylmercury in the various types of fish are found in the references at the end of this paper, and also at the FDA food safety Web site: www.cfsan.fda.gov/~frf/sea-mehg.html or the EPA Web site at www.epa.gov/ost/fish/. [FDA, EPA Revise Guidelines on Mercury in Fish FDA Consum. 2004 May-Jun;38(3):8-9.]

Safety of Vitamin D:

Too much vitamin D can be toxic, so as a rule, it is important to avoid chronically taking supplemental amounts over 1000 without checking with your physician. The vitamin D made in the skin by the sun is not as dangerous because the body limits how much active vitamin D is produced. However, one can take too much of the active form of vitamin D if it is included in several supplements in generous amounts.

The toxic level of vitamin D has traditionally been thought to be a chronic intake of 5 times the RDA of 400 iu, (i.e. 2000 iu,) so an intake of up to 1000 iu in the at-risk-of-inadequacy groups described above (and later) is clearly safe. In addition, there is new data suggesting that the toxicity level of this vitamin should actually be set considerably higher than 5 times the RDA, so there is even less cause for concern -- even if a multivitamin were taken by a four-glasses-of-milk-a-day California surfer! [Vitamin D supplementation, 25-hydroxyvitamin D concentrations, and safety. Am J Clin Nutr. **1999**;69(5):842-56.] **The health cost of inadequacy is much scarier, as is the surprisingly common finding of inadequate blood vitamin D levels when such assessments are actually made.**

Five Factors that Affect Vitamin D Adequacy

(References for all are at the end of this paper.)

1) The exposure of your skin to direct sun rays, and the condition of the skin.

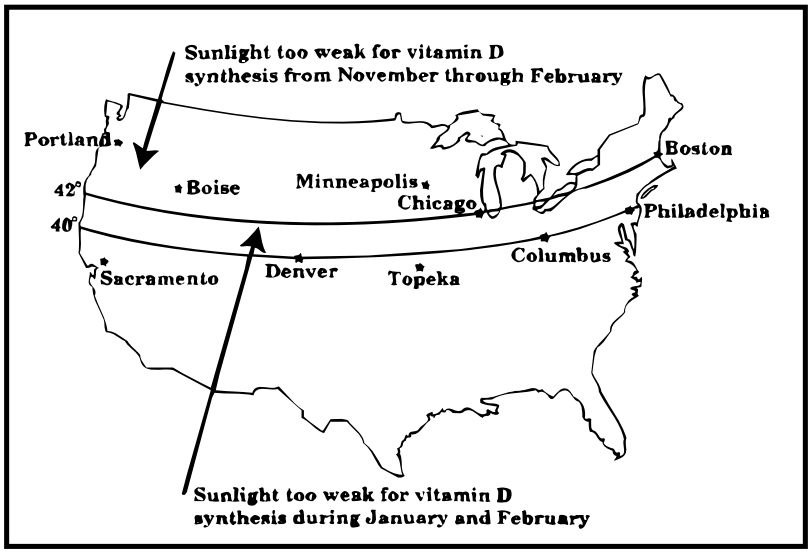
The major source of vitamin D is exposure to direct sunlight; our bodies make vitamin D in the skin. **The light coming through windows does not have the same effect.** Many people get plenty of vitamin D from light exposure so they do not need a supplement. On the other hand, **dermatologists recommend limiting sun exposure as a source of vitamin D**, because of risk of melanoma and they encouraging the use of oral supplementation instead. [*JAAD* **2005**;52(5): 868.] **In any case, the following situations may result in too little vitamin D production (especially in combination), so dietary vitamin D or a supplement may be needed:**

- **Clothing** There is a special risk among cultural/religious groups that cover nearly all the skin

surfaces, such as Catholic nuns who wear the old style habit, and many Muslim women. Studies have shown that inadequate vitamin D status is extremely common even among people who live in such sunny areas as the southern USA, Yemen, Saudi Arabia, Israel, Ethiopia, Turkey, Somalia and Lebanon in these circumstances.

- **Vitamin D Production from the Sun** (Tufts Health & Nutrition Newsletter 1996)

Living in the northern part of the country in the winter results in an inadequate angle of light rays to produce optimal amounts of vitamin D. At higher latitudes (starting about 40 degrees away from the equator,) there are fewer months of the year in which the sun's rays can cause enough vitamin D to be made. This is seen across North America, Asia, Europe, and in southern hemisphere countries like New Zealand. The same latitudinal relationships exist worldwide in relation to the incidence of the health problems described earlier. BMJ **1999**;318(7175) :39-40. European children and young adults often have circulating 25(OH)D levels in the insufficiency range during wintertime. [Vitamin D in preventive medicine: are we ignoring the evidence? Br J Nutr. **2003**;89(5):552-7.]



Vitamin D Production from the Sun
(Tufts Health & Nutrition Newsletter 1996)

- **Skin color** Melanin is both a skin-coloring substance and a filter that decreases absorption of

the UV light that causes vitamin D to be made in the skin. Dark skin makes less vitamin D with the same amount of light exposure.

- **Rarely going outdoors** A factor especially among the infirm or elderly; and remember that light coming through windows does not have the same ability to produce vitamin D. Among institutionalized people, 25(OH)D levels are quite often in the deficiency range.

- **Aging or injured skin** Elderly people have decreased ability to produce vitamin D in the skin even when there is generous exposure to the sun's rays. Elderly subjects have been shown to have average serum 25(OH)D levels in the insufficiency range throughout the year. Similarly, people whose skin has been severely burned appear to be less able to manufacture vitamin D.

- **Use of potent sunscreens** Using sunscreen is advisable to decrease a deadly skin cancer melanoma. Sunscreens block UV light so they will interfere with vitamin D production.

2) The amount of vitamin D in your usual diet.

As shown earlier, vitamin D is found naturally only in a few foods. Commercial dairies fortify milk, and one cup of fortified milk or fortified soy beverage provides about 100 iu of vitamin D. Milk "straight from the farm" provides no vitamin D. For most adults, 400 iu has been the dietary goal (that is, the goal for people with an "average" amount of sun exposure.) For people with little sun exposure or those living in the north, the intake goal is 800-1000 iu/day. A review of vitamin D issues in the Journal of Nutrition in 2005 noted that "even in countries that do fortify, vitamin D intakes are low in some groups due to their unique dietary patterns, such as low milk consumption, vegetarian diet, limited use of dietary supplements, or loss of traditional high fish intakes." Vitamin D intake: a global perspective of current status. J Nutr. **2005** Feb;135(2):310-6

3) The presence of vitamin D in any other vitamin supplements or nutritional products (including fortified cereals) taken regularly.

If you often take a multivitamin supplement that provides the RDA (Recommended Dietary Allowance) for vitamin D, it is unnecessary to use a calcium product with additional vitamin D **unless a higher amount is needed because of where you live, etc**. Situations in which higher than usual amounts are needed are described in section 1 above and in 4 and 5 below. Using a multivitamin also at least partially corrects the unrecognized poor vitamin D intake that can result when a person eats cheese, ice cream, yogurt but no milk, or uses unfortified or "raw" milk.

4) The use of certain medications increases the need for vitamin D.

Certain medications cause vitamin D to be used up more quickly, which greatly increases the risk of fractures and other problems. Many products to control seizures have this effect, especi-ally when a combination of medications is used. Some examples are phenobarbital, carbamaze-pine (Tegretol®), Valproate (Depakene®), and phenytoin (Dilantin®.) If regularly taking medica-tions of this kind, show this handout to your physician or registered dietitian and ask about the

advisability of taking extra vitamin D [Menopause and bone density issues for women with epilepsy. Neurology. **2003**;61(6 Suppl 2):S16-22. . Myopathy associated with anticonvulsant osteomalacia. BMJ. **1973**;4(5891):526-].

5) <u>Medical conditions</u> that may affect vitamin D and/or calcium requirements.

Some medical conditions will affect the need for vitamin D as well. Any condition that results in poor absorption of nutrients, especially those that affect absorption of fat, will increase the need for supplemental vitamin D. In addition, poor absorption of fat also decreases the absorption of calcium. Examples include cystic fibrosis, inflammatory bowel disease, and celiac disease, and especially so when the condition is poorly controlled. In these conditions, higher than average vitamin D intakes are often necessary for optimal health.

Certain kidney or liver diseases may make it necessary for you to take a special <u>form</u> of vitamin D called "calcitriol" for which a physician's prescription is needed. There is interest in this "active hormonal form" in some other conditions as well, such as certain forms of multiple sclerosis, and it is being used as an adjunct to chemotherapy for certain cancers. Requirements for calcium and vitamin D will also be increased when a person is trying to heal a fracture or treat osteoporosis. For any of these conditions, consult your physician and Registered Dietitian (RD) for specific guidance to assure that the amount of each nutrient you obtain from food and supplements is both adequate and safe.

<u>One way to remember all the major risk factors for vitamin D:</u>

Picture this person: "A lactose-intolerant, elderly African-American Nun who spends most of her day indoors, who takes medication for a seizure disorder, who uses sunscreen to prevent melanoma, and who lives in North Dakota." She has them all!

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